WHAT IS CLAIMED IS:

1. A water-soluble polymer having the structure:

$$POLY-[O]_b-C-NH-X-N$$

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II

wherein:

POLY is a water-soluble polymer segment,

b is 0 or 1,

X is a hydrolytically stable linker comprising at least 3 contiguous saturated carbon atoms, and

said polymer is absent aromatic groups and ester linkages.

2. The polymer of claim 1, wherein X is a saturated acyclic, cyclic or alicyclic hydrocarbon chain having a total of about 3 to about 20 carbon atoms.

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- 3. The polymer of claim 2, wherein X is a saturated acyclic, cyclic, or alicyclic hydrocarbon chain having a total number of carbon atoms selected from the group consisting of 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, and 20.
- 4. The polymer of claim 3, wherein X is a saturated acyclic, cyclic, or alicyclic hydrocarbon chain having a total number of carbon atoms selected from the group consisting of: from about 3 to about 20, from about 4 to about 12, from about 4 to about 10, and from about 5 to about 8 atoms.
- 5. The polymer of any one of claims 2 to 4, wherein X is a linear saturated acyclic hydrocarbon chain.

- 6. The polymer of claim 5, wherein X is a branched saturated acyclic hydrocarbon chain.
- 7. The polymer of claim 6, wherein X is branched at the carbon α to the maleimidyl group.
 - 8. The polymer of claim 6, wherein X is branched at the carbon β to the maleimidyl group.
- 10 9. The polymer of claim 6, wherein X is branched at the carbon γ to the maleimidyl group.
 - 10. The polymer of claim 5, having the structure:

$$POLY-[O]_b-C-NH-\begin{bmatrix}R^1\\I\\C\\R^2\end{bmatrix}_y$$

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wherein:

y is an integer from 1 to about 20;

III

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and

R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

- 11. The polymer of claim 10, wherein R¹ and R² in each occurrence is independently H or an organic radical selected from the group consisting of lower alkyl and lower cycloalkyl.
- 5 12. The polymer of claim 10, wherein R¹ and R² are both H, and Y is selected from the group consisting of 3, 4, 5, 6, 7, 8, 9, and 10.
 - 13. The polymer of claim 10 having the structure:

$$\begin{array}{c|c} O & & & & \\ & \parallel & & \\ POLY-[O]_b-C-NH- & & & \\ \hline & C & & C\alpha & \\ & \parallel & C & C\alpha & \\ & \parallel &$$

III-A

wherein at least one of R^1 or R^2 on C_{α} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and y is at least one.

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- 14. The polymer of claim 13, wherein each of R^1 and R^2 on C_{α} is independently selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.
- 20 15. The polymer of claim 13, wherein all other non- $C_{\alpha} R^1$ and R^2 variables are H.
 - 16. The polymer of claim 13 wherein at least one of R^1 or R^2 on C_{α} is lower alkyl or lower cycloalkyl.
- 25 17. The polymer of claim 13, wherein R^2 on C_{α} is H.

- 18. The polymer of claim 17, wherein R^1 on C_{α} is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, cyclopentyl, hexyl, and cyclohexyl.
- 5 19. The polymer of claim 13 having the structure:

POLY-
$$[O]_b$$
-C - NH $\begin{bmatrix} H \\ I \\ C \\ I \\ R^2 \end{bmatrix}$ $\begin{bmatrix} O \\ R^1 \\ R^2 \\ V-1 \end{bmatrix}$

III-B

wherein R¹ and R² is each independently alkyl or cycloalkyl.

20. The polymer of claim 13, having the structure:

POLY-[O]_b-C - NH
$$=$$
 $\begin{bmatrix} H \\ I \\ C \\ H \end{bmatrix}$ $\begin{bmatrix} R^1 \\ I \\ C \\ R^2 \\ y-1 \end{bmatrix}$

III-B

wherein R¹ is alkyl or cycloalkyl and and R² is H.

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- 21. The polymer of claim 19 wherein R^1 and R^2 are each independently either methyl or ethyl.
- 22. The polymer of claim 19, wherein R^1 and R^2 are the same.

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23. The polymer of claim 1, wherein said polymer possesses a hydrolytically stabilized maleimide ring.

24. The polymer of claim 8 having the structure:

POLY-[O]_b-C - NH
$$=$$

$$\begin{bmatrix}
H \\
I \\
I \\
C_{7} \\
C_{6} \\
C_{6}
\end{bmatrix}$$

$$\begin{bmatrix}
C_{6} \\
C_{4} \\
C_{7} \\
I \\
R^{2} \\
H
\end{bmatrix}$$

III-C

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wherein R^1 and R^2 is each independently selected from the group consisting of H, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, but are not both H, and

y is at least 2.

- 25. The polymer of claim 24, wherein R^1 and R^2 is each independently H, lower alkyl or lower cycloalkyl.
- 26. The polymer of claim 25, wherein R¹ and R² is each independently selected from the group consisting of H, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl, cyclopentyl, hexyl, and cyclohexyl.
 - 27. The polymer of claim 24, wherein R² is H.
- 20 28. The polymer of claim 10, having the structure:

POLY-
$$[O]_{b}$$
-C-NH $=$

$$\begin{bmatrix}
R_{1} \\
I \\
C \\
I \\
C_{T} \\
C_{T} \\
C_{B_{2}} \\
R_{2} \\
R_{2} \\
R_{2}
\end{bmatrix}$$
 $\begin{bmatrix}
R_{1} \\
R_{1} \\
I \\
I \\
R_{2} \\
R_{2}
\end{bmatrix}$
 $\begin{bmatrix}
R_{1} \\
R_{1} \\
I \\
I \\
I \\
R_{2}
\end{bmatrix}$
 $\begin{bmatrix}
R_{1} \\
R_{1} \\
I \\
I \\
R_{2}
\end{bmatrix}$
 $\begin{bmatrix}
R_{1} \\
R_{1} \\
I \\
I \\
I \\
I \\
R_{2}
\end{bmatrix}$

III-D

wherein at least one of R^1 and R^2 attached to C_γ is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

- 5 29. The polymer of claim 28, wherein at least one of R^1 and R^2 attached to C_{γ} is alkyl or cycloalkyl and all other R^1 and R^2 variables are H.
 - 30. The polymer of claim 28, wherein one of the R^1 variables attached to C_{α} or C_{β} is alkyl or cycloalkyl, and all other R^1 and R^2 variables are H.
 - 31. The polymer of claim 2, wherein X is a saturated cyclic or alicyclic hydrocarbon chain.
 - 32. The polymer of claim 31, wherein X has the structure:

$$\begin{bmatrix}
R^{1} \\
I \\
C \\
R^{2}
\end{bmatrix}_{q} CYC_{a} \begin{bmatrix}
R^{1} \\
C \\
R^{2}
\end{bmatrix}_{p_{q}}$$

$$IV$$

and

CYC_a is a cycloalkylene group having "a" ring carbons, where the value of "a" ranges from 3 to 12;

p and q are each independently 0 to 20, and p +q + a \leq 20,

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and

R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

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- 33. The polymer of claim 32, wherein p and q are each independently selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, and 8.
- The polymer of claim 32, wherein R¹, in each occurrence, is independently H or an organic radical that is either lower alkyl or lower cycloalkyl, and R², in each occurrence, is independently H or an organic radical that is either lower alkyl or lower cycloalkyl.
- 10 35. The polymer of claim 32, wherein a is selected from the group consisting of 5, 6, 7, 8 and 9.
 - 36. The polymer of claim 35, wherein a is 6 and CYC_a is a 1,1-, 1,2-, 1,3- or 1,4- substituted cyclohexyl ring.
 - 37. The polymer of claim 32, wherein p and q each independently range from 0 to 4.
 - 38. The polymer of claim 36, wherein the substituents on said substituted cyclohexyl ring are cis.
 - 39. The polymer of claim 36, wherein the substituents on said substituted cyclohexyl ring are trans.
 - 40. The polymer of claim 32, wherein R^1 and R^2 are H in every occurrence.
 - 41. The polymer of claim 34, having the structure:

POLY-
$$[O]_b$$
-C-NH- $(CH_2)_q$

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wherein q and p each independently range from 0 to 6.

- 42. The polymer of claim 41, wherein q ranges from 0 to 6 and p is zero.
- 43. The polymer of claim 34, having the structure:

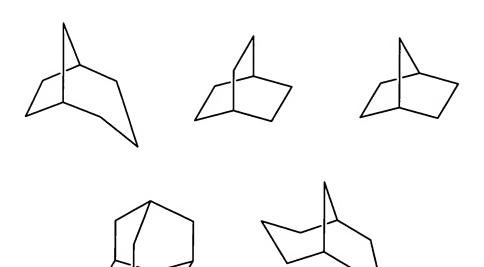
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POLY-
$$[O]_b$$
-C-NH- $(CH_2)_q$ $(CH_2)_p$ -N

wherein q and p each independently range from 0 to 6, and the substituents on the cyclohexylene ring are either cis or trans.

- 44. The polymer of claim 32, wherein CYC_a is bicyclic or tricyclic.
- 45. The polymer of claim 44, wherein CYC_a is selected from the group consisting of:



and said ring substituents are positioned at any available position on the bi or tricyclic ring.

5 46. The polymer of claim 1 having the structure:

$$\begin{array}{c|c}
O & O & O \\
O & O &$$

V

wherein X and b are as previously defined,

b' is 0 or 1, and

X' is a hydrolytically stable linker comprising at least 3 contiguous saturated carbon atoms.

- 15 47. The polymer of claim 1, wherein POLY is selected from the group consisting of a poly(alkylene oxide), poly(vinyl pyrrolidone), poly(vinyl alcohol), polyoxazoline, poly(acryloylmorpholine), and poly(oxyethylated polyol).
 - 48. The polymer of claim 47, wherein POLY is a poly(alkylene oxide).

49. The polymer of claim 48, wherein POLY is a poly(ethylene glycol).

50. The polymer of claim 49, wherein the poly(ethylene glycol) is terminally capped with an end-capping moiety.

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- 51. The polymer of claim 50, wherein the end-capping moiety is independently selected from the group consisting alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, alkynyloxy, substituted alkynyloxy, aryloxy, and substituted aryloxy.
- 5 52. The polymer of claim 51, wherein the end-capping moiety is selected from the group consisting of methoxy, ethoxy, and benzyloxy.
 - 53. The polymer of claim 49, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 100 daltons to about 100,000 daltons.
 - 54. The polymer of claim 53, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 1,000 daltons to about 50,000 daltons.
- 55. The polymer of claim 54, wherein the poly(ethylene glycol) has a nominal average molecular mass of from about 2,000 daltons to about 30,000 daltons.
 - 56. The polymer of claim 46, wherein said POLY is linear and the polymer is homobifunctional.
- 57. The polymer of claim 49, wherein said poly(ethylene glycol) has a structure selected from the group consisting of linear, branched and forked.
 - 58. The polymer of claim 26, wherein said poly(ethylene glycol) comprises the structure:

$Z-(CH_2CH_2O)_n-CH_2CH_2-$

where n is from about 10 to about 4000, and Z comprises a moiety selected from the group consisting of hydroxy, amino, ester, carbonate, aldehyde, aldehyde hydrate, acetal, ketone, ketone hydrate, ketal, alkenyl, acrylate, methacrylate, acrylamide, sulfone, thiol, carboxylic acid, isocyanate, isothiocyanate, hydrazide, urea, maleimide,

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vinylsulfone, dithiopyridine, vinylpyridine, iodoacetamide, alkoxy, benzyloxy, silane, lipid, phospholipid, biotin, and fluorescein.

59. The polymer of claim 1, corresponding to the structure:

$$R \left[\begin{array}{c} O \\ POLY-[O]_b-C-NH-X-N \\ O \end{array} \right]_d$$

VI

wherein:

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d is an integer from 3 to about 100, and

- R is a residue of a central core molecule having 3 or more hydroxyl groups, amino groups, or combinations thereof.
 - 60. The polymer of claim 59, wherein d is an integer from 3 to about 12.
- 15 61. The polymer of claim 1, wherein POLY is a multi-arm polymer segment, and said polymer corresponds to the structure:

where

PEG is -(CH₂CH₂O)_nCH₂CH₂-,

M is:

and m is selected from the group consisting of 3, 4, 5, 6, 7, and 8.

5 62. A water-soluble polymer having the structure:

POLY-
$$[O]_b$$
-C – NH— X—NH₂
VIII

wherein

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POLY is a water-soluble polymer segment,

b is 0 or 1,

X is a hydrolytically stable linker comprising at least 3 contiguous saturated carbon atoms,

and

said polymer is absent aromatic groups and ester linkages.

- 63. The polymer of claim 62, wherein X is a saturated acyclic, cyclic or alicyclic hydrocarbon chain having a total of about 3 to about 20 carbon atoms.
- 20 64. The polymer of claim 62, wherein X is a saturated acyclic, cyclic, or alicyclic hydrocarbon chain having a total number of carbon atoms selected from the group consisting of 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, and 20.
- 65. The polymer of claim 64, wherein X is a saturated acyclic, cyclic, or alicyclic
 25 hydrocarbon chain having a total number of carbon atoms selected from the group
 consisting of: from about 3 to about 20, from about 4 to about 12, from about 4 to about
 10, and from about 5 to about 8 atoms.

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- 66. The polymer of claim 63, wherein X is a linear saturated acyclic hydrocarbon chain.
- 5 67. The polymer of claim 63, wherein X is a branched saturated acyclic hydrocarbon chain.
 - 68. The polymer of claim 67, wherein X is branched at the carbon α to the maleimidyl group.

69. The polymer of claim 67, wherein X is branched at the carbon β to the maleimidyl group.

- 70. The polymer of claim 67, wherein X is branched at the carbon γ to the maleimidyl
 group.
 - 71. The polymer of claim 63, having the structure:

$$POLY-[O]_b-C-NH-\begin{bmatrix}R^1\\I\\C\\R^2\end{bmatrix}_yNH_2$$

20 VIII-A

wherein:

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y is an integer from 1 to about 20;

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and

R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

- 5 72. The polymer of claim 62, wherein X is a saturated cyclic or alicyclic hydrocarbon moity.
 - 73. The polymer of claim 72, wherein X has the structure:

$$\begin{bmatrix}
R^1 \\
C \\
C \\
R^2
\end{bmatrix} CYC_a \begin{bmatrix}
R^1 \\
C \\
R^2
\end{bmatrix}$$

$$Q$$

$$P$$

VIII-B

and

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 \mbox{CYC}_a is a cycloalkylene group having "a" ring carbons, where the value of "a" ranges from 3 to 12;

p and q are each independently 0 to 20, and p +q + a \leq 20,

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and

R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

- 74. The polymer of claim 73, wherein p and q are each independently selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, and 8.
 - 75. The polymer of claim 73, wherein R^1 , in each occurrence, is independently H or an organic radical that is either lower alkyl or lower cycloalkyl, and R^2 , in each

UTILITY PATENT

occurrence, is independently H or an organic radical that is either lower alkyl or lower cycloalkyl.

- 76. The polymer of claim 73, wherein a is selected from the group consisting of 5, 6, 5, 8, and 9.
 - 77. The polymer of claim 76, wherein a is 6 and CYC_a is a 1,1-, 1,2-, 1,3- or 1,4-substituted cyclohexylene ring.
- 10 78. The polymer of claim 77, having the structure:

POLY-
$$[O]_b$$
- C - NH - $(CH_2)_q$ - NH_2

wherein q and p each independently range from 0 to 6, and the substituents on said cyclohexylene ring are either cis or trans.

79. The polymer of claim 77, having the structure:

$$\begin{array}{c} O \\ \parallel \\ POLY-[O]_b-C-NH-(CH_2)_q \end{array} \\ \begin{array}{c} (CH_2)_p-NH_2 \end{array}$$

20 VIII-D

wherein q and p each independently range from 0 to 6, and the substituents on said cyclohexylene ring are either cis or trans.

- 80. The polymer of claim 73, wherein CYC_a is bicyclic or tricyclic.
- 81. A method for forming a maleimide terminated polymer, said method comprising the steps of:

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- a. reacting POLY-[O]_b-C(O)-LG (IX) with NH₂-X-NH₂ (XII) under conditions effective to form POLY-[O]_b-C(O)-H₂N-X-NH₂ (X), and
- b. converting POLY-[O]_b-C(O)-H₂N-X-NH₂ (**X**)into POLY-[O]_b-C(O)-HN-X-5 MAL (**II**),

wherein:

POLY is a water-soluble polymer segment,

b is 0 or 1,

X is a hydrolytically stable linker comprising at least 3 contiguous saturated carbon atoms,

LG is a leaving group,

MAL is maleimide,

and said maleimide terminated polymer is absent aromatic groups and ester linkages.

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- 82. The method of claim 81, wherein said LG is selected from the group consisting of halide, N-hydroxysuccinimide, N-hydroxybenzotriazole, para-nitrophenolate.
- 83. The method of claim 81, wherein one of said amino groups in said NH₂-X-NH₂ reagent is in protected form.
 - 84. The method of claim 81, wherein said reacting step is carried out in an organic solvent selected from the group consisting of acetonitrile, chloroform, dichloromethane, benzene, toluene, xylene, acetone, tetrahydrofuran (THF), dimethylformamide (DMF), and dimethylsulfoxide.
 - 85. The method of claim 81, wherein said reacting step is conducted under an inert atmosphere.
- 30 86. The method of claim 81, wherein said reacting step is conducted at a temperature in the range of about 0 to 100° C.

87. The method of claim 81, wherein said reacting step is conducted in the presence of a base selected from the group consisting of triethylamine, pyridine, 4-(dimethylamino)pyridine, and sodium carbonate.

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88. The method of claim 83, further comprising after said reacting step, deprotecting the amino group in POLY-[O]_b.C(O)-H₂N-X-NH₂.

89. The method of claim 81, further comprising the step of purifying the product from step (a) prior to said converting step.

- 90. The method of claim 89, wherein said purifying comprises purifying the product by column chromatography.
- 15 91. The method of claim 89, wherein said purifying comprises purifying the product by ion exchange chromatography.
 - 92. The method of claim 81, wherein said converting step comprises reacting POLY-[O]_b-C(O)-H₂N-X-NH₂ with a reagent selected from the group consisting of N-
- methoxycarbonylmaleimide, exo-7-oxa[2.2.1]bicycloheptane-2,3-dicarboxylic anhydride, and maleic anhydride under conditions suitable for forming POLY-[O]_b-C(O)-H₂N-X-MAL in a reaction mixture.
 - 93. The method of claim 92, wherein when said reagent is N-
- 25 methoxycarbonylmaleimide, and said converting step is carried out in water or an aqueous mixture of water and a water miscible solvent.
 - 94. The method of claim 92, wherein said reagent is maleic anhydride, and said converting step comprises reacting POLY-[O]_b-C(O)-H₂N-X-NH₂ with maleic anhydride under conditions effective to form POLY-[O]_b-C(O)- NH-X-NH-C(O)CH=CHCOOH (XI) as an intermediate, and said method further comprises:

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heating said POLY-[O]_b-C(O)-H₂N-X-NH-C(O)CH=CHCOOH under conditions effective to promote cyclization by elimination of water to form POLY-[O]_b-C(O)- NH-X-MAL.

- 5 95. The method of claim 92, further comprising recovering said POLY-[O]_b-C(O)-H₂N-X-MAL from the reaction mixture.
 - 96. The method of claim 95, wherein said recovered POLY- $[O]_b$ -C(O)- H_2N -X-MAL has a purity of greater than about 80 %.
 - 97. The method of claim 81, wherein X is a saturated acyclic, cyclic or alicyclic hydrocarbon chain having a total of about 3 to about 20 carbon atoms.
- 98. The method of claim 81, wherein X is a linear saturated acyclic hydrocarbon chain.
 - 99. The method of claim 81, wherein X is a branched saturated acyclic hydrocarbon chain.
- 20 100. The method of claim 99, wherein X is branched at the carbon α to the maleimidyl group.
 - 101. The method of claim 99, wherein \boldsymbol{X} is branched at the carbon $\boldsymbol{\beta}$ to the maleimidyl group.
 - 102. The method of claim 99, wherein X is branched at the carbon γ to the maleimidyl group.
 - 103. The method of claim 81, wherein said NH₂-X-NH₂ corresponds to the structure:

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$$H_2N = \begin{bmatrix} R_1 \\ I \\ C \\ R_2 \end{bmatrix}_y$$

XII-A

wherein

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y is an integer from 1 to about 20;

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl and

R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

104. The method of claim 81, wherein said NH₂-X-NH₂ corresponds to the structure:

$$H_2N = \begin{bmatrix} R^1 \\ I \\ C \\ I \\ R^2 \end{bmatrix}_q CYC_a = \begin{bmatrix} R^1 \\ I \\ C \\ R^2 \end{bmatrix}_{p} NH_2$$

XII-B

15 and

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 CYC_a is a cycloalkylene group having "a" ring carbons, where the value of "a" ranges from 3 to 12;

p and q are each independently 0 to 20, and p +q + $a \le 20$,

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and

R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

UTILITY PATENT

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- 105. A conjugate formed by reaction of a biologically active agent with the polymer of claim 1.
- 5 106. A conjugate comprising the following structure:

wherein:

POLY is a water-soluble polymer segment,

b is 0 or 1,

X is a hydrolytically stable linker comprising at least 3 contiguous saturated carbon atoms,

15 "POLY-[O]_b-C(O)-NH-X-" is absent aromatic groups and ester linkages, and

"-S-biologically active agent" represents a biologically active agent comprising a thiol (-SH) group.

- 20 107. A composition comprising the conjugate of claim 106, wherein said composition comprises a single polymer conjugate species.
 - 108. A conjugate comprising the following structure:

$$POLY-[O]_b-C-NH-X$$
 biologically active agent

wherein:

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POLY is a water-soluble polymer segment, b is 0 or 1,

X is a hydrolytically stable linker comprising at least 3 contiguous saturated carbon atoms,

"POLY- $[O]_b$ -C(O)-NH-X-" is absent aromatic groups and ester linkages, and

"-NH-biologically active agent" represents a biologically active agent comprising an amino group.

109. A method for forming a polymer conjugate, said method comprising contacting a biologically active agent comprising a reactive thiol group, "HS-biologically active agent", with a polymer of claim 1, under conditions effective to promote formation of a polymer conjugate having the structure:

POLY-
$$[O]_b$$
-C-NH- X biologically active agent

- 110. The method of claim 109, wherein said contacting step is carried out at pHs ranging from about 6.0 to about 8.0.
- 111. The method of claim 110, wherein said polymer conjugate is formed in a reaction mixture, and said method further comprises after said contacting step, isolating said polymer conjugate from said reaction mixture.
- 25 112. A hydrogel formed using the water-soluble polymer of claim 1.
 - 113. A hydrogel formed using the water soluble polymer of claim 59.

- 114. A hydrogel formed using the water soluble polymer of claim 61.
- 115. A water soluble polymer having the structure:

XIII

wherein:

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POLY is a water-soluble polymer segment,

X is a hydrolytically stable linker that is a saturated cyclic or alicyclic hydrocarbon chain having a total of about 3 to about 20 carbon atoms,

and

said polymer is absent aromatic groups and ester linkages.

116. The polymer of claim 115, wherein X has the structure:

$$\begin{bmatrix}
R^{1} \\
C \\
C \\
R^{2}
\end{bmatrix}_{q} CYC_{a} \begin{bmatrix}
R^{1} \\
C \\
C \\
R^{2}
\end{bmatrix}_{p,}$$

XIII-A

and

CYC_a is a cycloalkylene group having "a" ring carbons, where the value of "a" ranges from 3 to 12;

p and q are each independently 0 to 20, and p +q + a \leq 20,

R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl, and

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R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkylenecycloalkyl, and substituted alkylenecycloalkyl.

- 5 117. The polymer of claim 116, wherein p and q are each independently selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, and 8.
 - 118. The polymer of claim 116, wherein R¹, in each occurrence, is independently H or an organic radical that is selected from the group consisting of lower alkyl, lower cycloalkyl, and lower alkylenecycloalkyl, and R², in each occurrence, is independently H or an organic radical that is selected from the group consisting of lower alkyl, lower cycloalkyl, and lower alkylenecycloalkyl.
- 119. The polymer of claim 116, wherein a is selected from the group consisting of 5, 6, 7, 8 and 9.
 - 120. The polymer of claim 116, wherein the substituents on CYC_a are cis.
 - 121. The polymer of claim 116, wherein the substituents on CYC_a are trans.
 - 122. The polymer of claim 119, wherein a is 6 and CYC_a is a 1,1-, 1,2-, 1,3- or 1,4-substituted cyclohexyl ring.
 - 123. The polymer of claim 116, wherein p and q each independently range from 0 to 4.
 - 124. The polymer of claim 116, wherein R¹ and R² are H in every occurrence.
 - 125. The polymer of claim 116, having the structure:

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POLY-O—
$$(CH_2)_q$$
 $(CH_2)_p$ $(CH_2)_p$ $(CH_2)_p$ $(CH_2)_p$ $(CH_2)_q$ $(C$

XIII-B

wherein q and p each independently range from 0 to 6.

- 5 126. The polymer of claim 116, wherein q ranges from 0 to 6 and p is zero.
 - 127. The polymer of claim 116, having the structure:

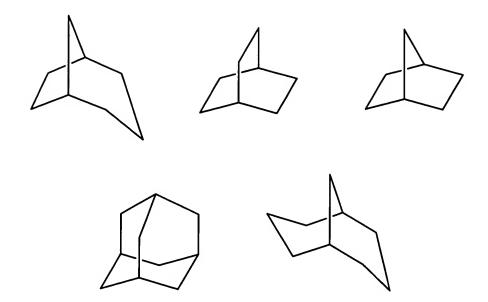
POLY-O—
$$(CH_2)_q$$
 $(CH_2)_p$ N

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XIII-C

wherein q and p each independently range from 0 to 6.

- 128. The polymer of claim 116, wherein CYC_a is bicyclic or tricyclic.
- 15 129. The polymer of claim 116, wherein CYC_a is selected from the group consisting of:



and said ring substituents are positioned at any available position on the bi or tricyclic ring.

130. A method for forming a maleimide terminated polymer, said method comprising:

a. reacting POLY- $[O]_b$ -C(O)-LG with H_2N -X-MAL under conditions effective to form POLY- $[O]_b$ -C(O)-HN-X-MAL,

wherein:

POLY is a water-soluble polymer segment,

b is 0 or 1,

X is a hydrolytically stable linker comprising at least 3 contiguous saturated carbon atoms,

LG is a leaving group,

MAL is maleimide,

and said maleimide terminated polymer is absent aromatic groups and ester linkages.

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